Information

Etiology and Pathogenesis Of Hypertension

HARRIET P. DUSTAN, M.D.

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HYPERTENSION is a major cardiovascular problem that is largely unsolved. However, there are a variety of drugs available for treatment which used singly or in combination reduce arterial pressure substantially. Such therapeutic effectiveness tends to obscure the fact that we actually know very little about the mechanisms of hypertension and the functional details of its natural history.

Hypertension is a symptom, not a disease. We know it to be associated with a variety of diseases, but these affect only a small number of patients so that in most hypertension is without apparent cause. This condition is called essential hypertension. The term is an archaic misnomer because we know that hypertension is not essential for anything. Long gone are the days when physicians believed elevated arterial pressure to be essential for maintenance of tissue perfusion.

Although elevated blood pressure, of itself, is a symptom, it is often associated with vascular diseases—arteriolar sclerosis or premature atherosclerosis. Arteriolar disease occurs more commonly in patients with severe diastolic hypertension, while premature atherosclerosis is usually a manifestation of long sustained arterial pressure elevation, even one of mild degree.

Hypertension can be classified in a number of ways according to: (1) the type of arterial pressure elevation—systolic, diastolic, or mixed, (2) the character of the elevation—labile or sustained, (3) severity of the associated vascular disease—mild, moderate, severe, or malignant (accelerated), (4) or etiology—renal, adrenal, cardiovascular, or essential. At our present level of knowledge, the etiologic classification is the most interesting. Not only does recognition of the various causes of elevated arterial pressure lead to more rational treatment, but also it gives an opportunity to study the mechanisms of hypertension.

The hypertensions that are associated with various diseases are called secondary. When none of these conditions is present, the hypertension is said to be primary. This term, like "essential," is a misnomer because each hypertension has a cause even though our knowledge is not sufficient to recognize it. Clearly, the more we have learned the more we have seen; for example, consider the types of hypertension recognized in the past 20 years. These include primary aldosteronism, renal arterial disease, and increased activity of the beta-adrenergic component of the sympathetic nervous system. Before these types were recognized, such patients were considered to have "essential" or "primary" hypertension.

The physiologic abnormalities that have been found in hypertensives relate to the nervous control of the circulation, catecholamines, cardiac output and peripheral resistance, adrenal steroids, the renal pressor system and plasma volume. Evidence is accumulating that these factors do not operate alone, and it seems likely that they make up an integrated system, one expression of which is elevated blood pressure.

When considering the etiology and pathogenesis of hypertension, it is an interesting exercise to see how these various factors are interrelated in the different types of hypertension. Of course, our present information is incomplete, but enough is available to make the exercise worthwhile.

The most frequently occurring secondary hypertensions now recognized are those associated with renal arterial disease and renal parenchymal disease, pheochromocytoma, primary aldosteronism, coarctation of the aorta and increased activity of the beta-adrenergic nervous system.

In patients with renal arterial disease, the most likely cause of hypertension is, of course, the renin-angiotensin system. However, elevations of renin (which is the component most readily measured) are not routinely found. This suggests that other factors are also operating and since blood pressure can be lowered with drugs that suppress the activity of the sympathetic nervous system, this indicates a nervous component in the hypertension as well. In fact, we have recently shown that these patients often have exaggerated increases in blood pressure in response to head-up tilt. Further, they tend to have slightly increased cardiac output which may represent an increase in nervous stimulation

Dr. Dustan is from the Research Division, Cleveland Clinic, Cleveland, Ohio.

of the heart. Plasma volume can be decreased and, in our experience, it is inversely related to the plasma renin activity. Additionally, aldosterone production is often increased producing a state of secondary aldosteronism. Thus, although we cannot put together all the pieces of information in an integrated fashion, evidence is accumulating that the hypertension accompanying renal arterial disease is an expression of a variety of abnormalities, only one of which is a disturbance of the renin-angiotensin system.

In renal parenchymal disease, there is not so much information available concerning the possible pressor factors. However, there have been studies in patients with chronic renal failure which show expansion of the extracellular fluid volumes and correction of hypertension when these excesses are corrected by dialysis. Further, there is a suggestion that with expanded plasma volume the nervous control of the circulation is lessened—possibly because it isn't so necessary when the blood volume is high. Plasma renin activity has not been consistently found to be elevated although increased activity of the renin-angiotensin system seems likely in patients whose hypertension remits following bilateral nephrectomy done in preparation for transplantation. Thus, in this type of hypertension, there are indications that, in one way or another, three pressor factors participate—renal pressor, neurogenic, and fluid volume.

Pheochromocytoma seems a much more straightforward problem than that presented by the other two types of hypertension. Currently, we know that there is increased epinephrine and norepinephrine production, and this seems reason enough for the hypertension. Plasma volume can also be reduced, and this is important because it may explain the hypotensive crises that often occur in these patients following surgical removal of the tumor.

In primary aldosteronism, there is an increased production of aldosterone which can cause increases in body sodium, extracellular fluid volume and plasma volume. Along with these increases, decreased activity of the sympathetic nervous system has been reported. Plasma renin activity is low, suggesting that this is not a factor in the hypertension.

Increased activity of the beta-adrenergic component of the sympathetic nervous system can be associated with hypertension. These patients have palpitations and exaggerated tachycardia in response to a variety of normal stimuli, such as exercise. They have increased cardiac output but a normal or near normal peripheral resistance. Their hypertension can be controlled with beta-blocking drugs such as propranolol.

Coarctation of the aorta is also recognized as occasional cause of hypertension. If patients are not in cardiac failure, apparently hemodynamic functions are normal, at least in the upper parts of the body above the coarctation. However, until flow beyond the coarctation can be measured reliably, hemodynamic characteristics of this type of hypertension cannot be determined. Other pressor mechanisms have not been studied in such patients.

Although most treatments of hypertension are empiric rather than based on specific pressor mechanisms, information is becoming increasingly available in various types of hypertension which bids well to describe a number of integrated circulatory disturbances, of which hypertension is one manifestation. These descriptions will provide rational, rather than empiric, treatment.